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Substitute for form 1449B/PTO  
INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet

1

of

2

Complete if Known

Application Number	10/371,149	10/371,149
Filing Date	02/20/2002	11/14/03
First Named Inventor	Gunars E. Valkirs	et. al.
Group Art Unit	4632	1641
Examiner Name	L. Cool	
Attorney Docket Number	071949-5408	

U.S. PATENT DOCUMENTS

Examiner Initials*	Cite No. <sup>1</sup>	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number	Kind Code <sup>2</sup> (if known)			
L/C	A1	6,235,489 B1		Jackowski et al.	May 22, 2001	
L/C	A2	6,268,223 B1		Cornell-Bell et al.	July 31, 2001	

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No. <sup>1</sup>	Foreign Patent Document			Name of Patentee or Applicant of Cited Documents	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T <sup>6</sup>
		Office <sup>3</sup>	Number <sup>4</sup>	Kind Code <sup>5</sup> (if known)				
L/C	A3	WO	00/52476 A1		Skye Pharmatech Incorporated	Sept. 8, 2000		

OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>6</sup>
L/C	A4	Feinberg et al., "Guidelines for the Management of Transient Ischemic Attacks." Stroke, 25(6): 1320-1335, June 1994.	
	A5	Herrmann et al., "Release of Glial tissue-specific proteins after acute stroke: A comparison analysis of serum concentrations of protein S-100B and Glial fibrillary acidic protein." Stroke, 31:2670-2677, 2000.	
	A6	Napoli et al., "C-reactive protein in ischemic stroke: An independent prognostic factor." Stroke, 32:917-924, 2001.	
	A7	Strand et al., "Brain and plasma proteins in spinal fluid as markers for brain damage and severity of stroke." Stroke: 15(1): 138-144, 1994.	
L/C	A8	Hirashima et al., "Elevation of platelet activating factor, inflammatory cytokines, and coagulation factors in the internal jugular vein of patients with subarachnoid hemorrhage." Neurochemical Research, 22(10): 1249-1255, 1997.	

Examiner Signature

*L. Cool*

Date Considered

12/29/06

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		Filing Date	02/20/2002 11/14/03
		First Named Inventor	Gunars E. Valkirs et. al.
		Group Art Unit	1632 1641
		Examiner Name	L. Cook
(use as many sheets as necessary)		Attorney Docket Number	071949-5408
Sheet	2	of	2

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Examiner Signature	<i>Lisa L Cook</i>	Date Considered	12/29/06
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Substitute for form 1449B/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT  (use as many sheets as necessary)		Complete if Known	
		Application Number	10/225,082 10/24/02
		Filing Date	08/20/2002 11/14/03
		First Named Inventor	Gunars E. Valkirs et al.
		Group Art Unit	4632 1641
		Examiner Name	L. Cook
Sheet	1 of 21	Attorney Docket Number	071949-5408

### U.S. PATENT DOCUMENTS

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		Number	Kind Code <sup>2</sup> (if known)			
L/C	A1	5,114,923		Seilhamer et al.	May 19, 1992	
	A2	5,480,792		Buechler et al.	Jan. 2, 1996	
	A3	5,525,524		Buechler et al.	Jun. 11, 1996	
	A4	5,631,171		Sandstrom et al.	May 20, 1997	
	A5	5,679,526		Buechler et al.	Oct. 21, 1997	
	A6	5,824,799		Buechler et al.	Oct. 20, 1998	
	A7	5,851,776		Valkirs	Dec. 22, 1998	
	A8	5,885,527		Buechler	Mar. 23, 1999	
	A9	5,922,615		Nowakowski et al.	Jul. 13, 1999	
	A10	5,939,272		Buechler et al.	Aug. 17, 1999	
	A11	5,947,124		Buechler et al.	Sep. 7, 1999	
	A12	5,955,377		Maul et al.	Sep. 21, 1999	
	A13	5,985,579		Buechler et al.	Nov. 16, 1999	
	A14	6,019,944		Buechler	Feb. 1, 2000	
	A15	6,057,098		Buechler et al.	May 2, 2000	
	A16	6,113,855		Buechler et al.	Sep. 5, 2000	
	A17	6,143,576		Buechler	Nov. 7, 2000	

### FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No. <sup>1</sup>	Foreign Patent Document			Name of Patentee or Applicant of Cited Documents	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T <sup>6</sup>
		Office <sup>3</sup>	Number <sup>4</sup>	Kind Code <sup>5</sup> (if known)				
L/C	A18		WO 01/16599		Viotech Imaging, LLC	March 8, 2001		

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L/C	A19	Aggarwal et al., "Evaluation of serum lipid profile and cardiac enzyme changes in cerebrovascular accidents," JIMA, 93:331-332, 1995.	X

Examiner Signature	<i>Olivia X Cook</i>	Date Considered	12/29/06
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		Application Number	10/225,082 10/24/02
		Filing Date	08/20/2002 11/14/03
		First Named Inventor	Gunars E. Valkirs et. al.
		Group Art Unit	1632 1641
Examiner Name	L. Cook		
Sheet 2 of 21	Attorney Docket Number	071949-5408	

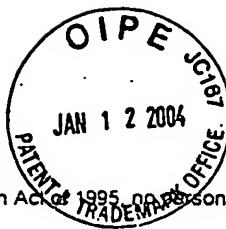
OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS			
Examiner Initials <sup>1</sup>	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>6</sup>
L/C	A20	Akiyama et al., "Changes in serum concentrations of matrix metalloproteins, tissue inhibitors of metalloproteinases and Type IV collagen in patients with various types of glomerulonephritis," Res. Commun. In Mol. Path. and Pharm., 95(2): 115-128, 1997.	
	A21	Albrecht et al., "Detection of circulating tissue factor and factor VII in a normal population," Thrombosis and Haemostasis, 75(5): 772-7, 1996.	
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	A23	Austgulen et al., "Increased maternal plasma levels of soluble adhesion molecules (ICAM-1, VCAM-1, E-selectin) in preeclampsia," Eur. J. Obstet. Gynecol. Reprod. Biol., 71:53-58, 1997.	
	A24	Banks et al., "Circulating intercellular adhesion molecule-1 (ICAM-1), E-selectin and vascular cell adhesion molecule-1 (VCAM-1) in human malignancies," Br. J. Cancer, 68:122-124, 1993.	
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	A26	Benamer et al., "Comparison of the prognostic value of C-reactive protein and troponin I in patients with unstable angina pectoris," Am. J. Cardiol., 82:845-850, 1998.	
	A27	Berendes et al., "Secretion of brain natriuretic peptide in patients with aneurysmal subarachnoid haemorrhage," Lancet, 349:245-249, 1997.	
	A28	Bialik et al., "Myocyte apoptosis during acute myocardial infarction in the mouse localizes to hypoxic regions but occurs independently of p53," J.Clin.Invest., 100(6): 1363-1372, 1997.	
	A29	Biasucci et al., "Elevated levels of interleukin-6 in unstable angina," Circulation, 94:874-877, 1996.	
L/C	A30	Biasucci et al., "Episodic activation of the coagulation system in unstable angina does not elicit an acute phase reaction," Am. J. of Cardiol., 77:85-87, 1996.	

Examiner Signature	<i>Olivia L. Cook</i>	Date Considered	12/29/06
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STATEMENT BY APPLICANT

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## Complete if Known

Application Number	10/225,062 10/21/03
Filing Date	08/20/2002 11/14/03
First Named Inventor	Gunars E. Valkirs G. V.
Group Art Unit	1632 1641
Examiner Name	L. Cook
Attorney Docket Number	071949-5408

Sheet 3 of 21

## OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS

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WC	A31	Biasucci et al., "Increasing levels of interleukin (IL)-1Ra and IL-6 during the first 2 days of hospitalization in unstable angina are associated with increased risk of in-hospital coronary events," Circulation, 99:2079-2084, 1999.	
	A32	Bitsch et al., "A longitudinal prospective study of soluble adhesion molecules in acute stroke," Stroke, 29:2129-2135, 1998.	
	A33	Blankaert et al., "Constitutive release of metalloproteinase-9 (92-kd Type IV collagenase) by Kaposi's sarcoma cells," J. Acquir. Immune Defic. Syndr. Hum. Retrovirol., 18:203-209, 1998.	
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	A35	Bollensen et al., "Adenylate kinase enzyme activity in cases of brain infarction," Acta Neurol. Scand., 79:53-58, 1989.	
	A36	Bonfrer et al., "The luminescence immunoassay S-100: a sensitive test to measure circulating S-100B: its prognostic value in malignant melanoma," Brit. Jour. Of Cancer, 77(12): 2210-2214, 1998.	
	A37	Bonow, "New insights into the cardiac natriuretic peptides," Circulation, 93:1946-1950, 1996.	
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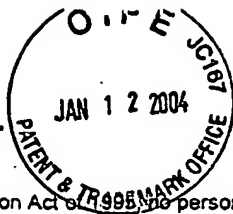
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		Application Number	10/225,002 10/214,078
		Filing Date	08/20/2002 11/14/03
		First Named Inventor	Gunars E. Valkirs et al.
		Group Art Unit	4632 1641
		Examiner Name	L. COOL
Sheet	4	of	21
		Attorney Docket Number	071949-5408

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LWC	A39	Caligiuri et al., "Immune system activation follows inflammation in unstable angina: pathogenetic implications," J.Am. Coll. Cardiol., 32:1295-1304, 1998.	
	A40	Carlstedt et al., "Proinflammatory cytokines, measured in a mixed population on arrival in the emergency department, are related to mortality and severity of disease," Journal of Internal Medicine; 242:361-365, 1997.	
	A41	Carter et al., "Platelet GP IIIa P1A and GP Ib variable number tandem repeat polymorphisms and markers of platelet activation in acute stroke," Arterioscler Thromb. Vasc. 18:1124-1131, 1998.	
	A42	Carter et al., "Purification, cloning, expression and biological characterization of an interleukin-1 receptor antagonist protein," Nature, 344:633-638, 1990.	
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	A45	Dangas et al., "Correlation of serum lipoprotein(a) with the angiographic and clinical presentation of coronary artery disease," Am. J. Cardiol., 83:583-585, 1999.	
LWC	A46	Davie et al., "The coagulation cascade: initiation, maintenance and regulation," Biochemistry, 30(43): 10363-10370, 1991.	

Examiner Signature	Olivia L. Cook	Date Considered	12/29/06
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		First Named Inventor	Gunars E. Valkirs et al.
		Group Art Unit	1632-1641
		Examiner Name	L. Cook
Sheet	5	of	21
		Attorney Docket Number	071949-5408

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L/C	A47	DeRose et al., "Circulating adhesion molecules in cystic fibrosis," Am. J. Respir. Crit. Care Med., 157: 1234-1239, 1998.	
	A48	Eisenberg et al., "Interleukin 1 receptor antagonist is a member of the interleukin 1 gene family: evolution of a cytokine control mechanism," Proc. Nat. Acad. Sci. USA, 88: 5232-5236, 1991.	
	A49	Emsley et al., "Crystal structure of the von Willebrand factor A1 domain and implications for the binding of platelet glycoprotein Ib," Journal of Biological Chemistry, 273(17): 10396-10401, 1998.	
	A50	Endo et al., "Elevated levels of serum and plasma metalloproteinases in patients with gastric cancer," Anticancer Research, 17:2253-2258, 1997.	
	A51	Estrada et al., "High plasma levels of endothelin-1 and atrial natriuretic peptide in patients with acute ischemic stroke," Am. J. of Hypertension, 7(12): 1085-1089, 1994.	
	A52	Fassbender et al., "Proinflammatory cytokines in serum of patients with acute cerebral ischemia: kinetics of secretion and relation to the extent of brain damage and outcome of disease," Journal of the Neurological Sciences, 122:135-139, 1994.	
	A53	Feinberg et al., "Hemostatic markers in acute ischemic stroke," Stroke, 27:1296-1300, 1996.	
L/C	A54	Fernandes-Alnemri et al., "CPP32, a novel human apoptotic protein with homology to <i>Caenorhabditis elegans</i> cell death protein Ced-3 and mammalian interleukin-1 $\beta$ -converting enzyme," Journal of Biological Chemistry, 269(49): 30761-30764, 1994.	

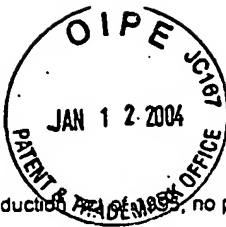
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Substitute for form 1449B/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT  (use as many sheets as necessary)		Complete if Known	
		Application Number	10/225,082 10/214,078
		Filing Date	08/20/2002 11/14/03
		First Named Inventor	Gunars E. Valkirs Jr. et al.
		Group Art Unit	1632 1641
		Examiner Name	L. Goolsby
Sheet	6	of	21
		Attorney Docket Number	071949-5408

OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>2</sup>
LVC	A55	Fisher et al., "Serum concentrations and peripheral secretion of the beta chemokines monocyte chemoattractant protein 1 and macrophage inflammatory protein 1 $\alpha$ in alcoholic liver disease," Gut, 45(3): 416-420, 1999.	
	A56	Fon et al., "Hemostatic markers in acute transient ischemic attacks," Stroke, 25(2): 282-286, 1994.	
	A57	Fujii et al., "Hemostasis in spontaneous subarachnoid hemorrhage," Neurosurgery, 37(2): 226-234, 1995.	
	A58	Fujii et al., "Serial changes of hemostasis in aneurysmal subarachnoid hemorrhage with special reference to delayed ischemic neurological deficits," J.Neurosurg., 86:594-602, 1997.	
	A59	Fujii et al., "Hemostasis in spontaneous subarachnoid hemorrhage," Neurosurgery, 37(2): 226-234, 1995.	
	A60	Gabay et al., "Interleukin-1 receptor antagonist (IL-1Ra) is an acute-phase protein," J.Clin. Invest., 99(12): 2930-2940, 1997.	
	A61	George et al., "Evidence for altered hepatic matrix degradation in genetic haemochromatosis," Gut, 42: 715-720, 1998.	
LVC	A62	Gohji et al., "Elevation of serum levels of matrix metalloproteinase-2 and -3 as new predictors of recurrence in patients with urothelial carcinoma," Circulation, 99:608-613, 1999.	

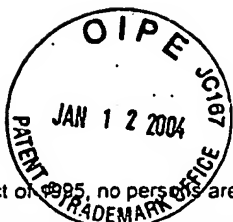
Examiner Signature	<i>Olivia L. Cook</i>	Date Considered	12/29/06
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		First Named Inventor	Gunars E. Valkirs J.E. G.
		Group Art Unit	4632 1641
		Examiner Name	L. Cook
Sheet	7	of	21
		Attorney Docket Number	071949-5408

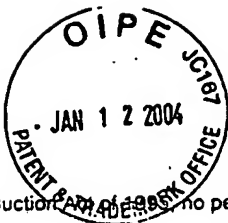
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	A68	Heinrich et al., "Association of variables of coagulation, fibrinolysis and acute-phase with atherosclerosis in coronary and peripheral arteries and those arteries supplying the brain," Thrombosis and Haemostasis, 73(3): 374-379, 1995.	
	A69	Hirashima et al., "Elevation of platelet activating factor, inflammatory cytokines, and coagulation factors in the internal jugular vein of patients with subarachnoid hemorrhage," Neurochem. Res., 22: 1249-1255, 1997.	
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		First Named Inventor	Gunars E. Valkirs J.E. ad.
		Group Art Unit	4632 1641
		Examiner Name	L. Cook
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		Attorney Docket Number	071949-5408

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	A75	James, T., "The variable morphological coexistence of apoptosis and necrosis in human myocardial infarction: significance for understanding its pathogenesis, clinical course, diagnosis and prognosis," Coron. Artery Dis., 9:291-307, 1998.	
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	A77	Johnson et al., "Activation of matrix-degrading metalloproteinases by mast cell proteases in atherosclerotic plaques," Arterioscler. Thromb. Vasc. Biol., 18:1707-1715, 1998.	
LVC	A78	Johnsson, "Markers of cerebral ischemia after cardiac surgery," J. Cardiothorac. Vasc. Anesth., 10: 120-126, 1996	

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		Filing Date	08/20/2002 11/14/03
		First Named Inventor	Gunars E. Valkirs et al.
		Group Art Unit	1632 1641
		Examiner Name	LCOOLC
Sheet	9	of	21
		Attorney Docket Number	071949-5408

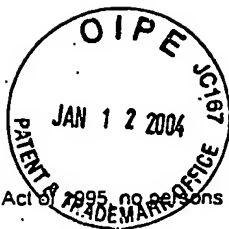
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LKC	A79	Jougasaki et al., "Adrenomedullin: potential in physiology and pathophysiology," Life Sciences, 66(10): 855-872, 2000.	
	A80	Kaneko et al., "Circulating levels of $\beta$ -chemokines in systemic lupus erythematosus," J. Rheumatol., 26: 568-573, 1999.	
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	A85	Kim, "Cytokines and adhesion molecules in stroke and related diseases," J.Neurol. Sci., 137:69-78, 1996.	
LKC	A86	Kim et al., "Kidney as a major clearance organ for recombinant human interleukin-1 receptor antagonist," J.Pharm. Sci., 84:575-580, 1995.	

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		First Named Inventor	Gunars E. Valkirs
		Group Art Unit	1632 1141
		Examiner Name	L. COOK
Sheet	10	of	21
		Attorney Docket Number	071949-5408

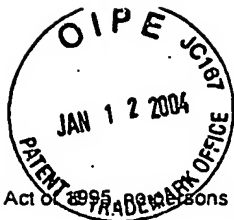
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	A88	Koyama et al., "Determination of plasma tissue factor antigen and its clinical significance," Br. J. Haematol., 87:343-347, 1994.	
	A89	Krupinski et al., "Protein kinase expression and activity in the human brain after ischaemic stroke," Acta Neurobiol. Exp. 58:13-21, 1998.	
	A90	Kudo et al., "Clearance and tissue distribution of recombinant human interleukin 1 $\beta$ in rats," Cancer Res., 50:5751-5755, 1990.	
	A91	Kuwasako et al., "Increased plasma proadrenomedullin N-terminal 20 peptide in patients with essential hypertension," Ann. Clin. Biochem., 36:622-628, 1999.	
	A92	Landi et al., Hypercoagulability in acute stroke: prognostic significance." Neurol., 37: 1667-1671, 1987.	
	A93	Laskowitz et al., "Serum markers of cerebral ischemia," J.Stroke Cerebrovasc. Dis., 7:234-241, 1998	
LVC	A94	Latini et al., "Cytokines in acute myocardial infarction: selective increase in circulating tumor necrosis factor, its soluble receptor, and interleukin-1 receptor antagonist," J.Cardiovasc. Pharmacol., 23:1-6, 1994.	

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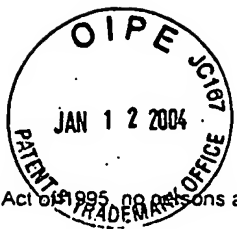
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LVC	A102	Long et al., "p53 and the hypoxia-induced apoptosis of cultured neonatal rat cardiac myocytes," J. Clin. Invest., 99:2635-2643, 1997.	

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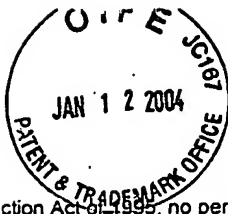
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Substitute for form 1449B/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT  (use as many sheets as necessary)		Complete if Known	
		Application Number	10/225,082 10/21/02
		Filing Date	08/20/2002 11/14/03
		First Named Inventor	Gunars E. Valkirs et al.
		Group Art Unit	1632 1641
		Examiner Name	L. Cook
Sheet	13	of	21
		Attorney Docket Number	071949-5403

OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>6</sup>
LVC	A111	McKeating et al., "Transcranial cytokine gradients in patients requiring intensive care after acute brain injury," Br. J. Anaesth., 78:520-523, 1997.	
	A112	Missler et al., "S-100 protein and neuron-specific enolase concentrations in blood as indicators of infarction volume and prognosis in acute ischemic stroke," Stroke, 28, 1956-1960, 1997.	
	A113	Miyata et al., "Conformational changes in the A1 domain of von Willebrand factor modulating the interaction with platelet glycoprotein Iba," Biol. Chem., 271:9046-9053, 1996.	
	A114	Montalescot et al., "Early increase of von Willebrand factor predicts adverse outcome in unstable coronary artery disease," Circulation, 98:294-299.	
	A115	Moore et al., "Collagenase expression in ovarian cancer cell lines," Gynecol. Oncol., 65:78-82, 1997.	
	A116	Mori et al., "Vasodilator effects of C-type natriuretic peptide on cerebral arterioles in rats," Eur. J. Pharmacol., 320:183-186, 1997.	
	A117	Mowla et al., "Biosynthesis and post-translational processing of the precursor to brain-derived neurotrophic factor," J. Biol. Chem., 276: 12660-12666, 2001.	
LVC	A118	Mun-Bryce and Rosenberg, "Matrix metalloproteinases in cerebrovascular disease," J. Cereb. Blood Flow Metab., 18:1163-1172, 1998.	

Examiner Signature	<i>Lisa J. Cook</i>	Date Considered	12/29/06
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(use as many sheets as necessary)		Filing Date	08/20/2002 11/14/03
		First Named Inventor	Gunars E. Valkirs et al.
		Group Art Unit	4632 1641
		Examiner Name	L. Cook
Sheet	14	of	21
		Attorney Docket Number	071949-5408

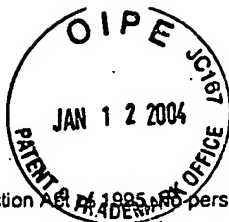
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LVC	A119	Niebroj-Dobosz et al., "Immunochemical analysis of some proteins in cerebrospinal fluid and serum of patients with ischemic strokes." Folia Neuropathol., 32: 129-137, 1994.	
	A120	Nishiyama et al., "Simultaneous elevation of the levels of circulating monocyte chemoattractant protein-1 and tissue factor in acute coronary syndromes," Jpn. Circ. J., 62:710-712, 1998.	
	A121	Nishizawa et al., "Protein kinase C $\delta$ and $\alpha$ are involved in the development of vasospasm after subarachnoid hemorrhage," Eur. J. Pharmacol., 398: 113-119, 2000.	
	A122	Ohtsuka et al., "Clinical implications of circulating soluble Fas and Fas ligand in patients with acute myocardial infarction," Coron. Artery Dis., 10:221-225, 1999.	
	A123	Oltrona et al., "C-Reactive protein elevation and early outcome in patients with unstable angina pectoris," Am. J. Cardiol., 80:1002-1006, 1997.	
	A124	Otsuki et al., "Circulating vascular cell adhesion molecule-1 (VCAM-1) in atherosclerotic NIDDM patients," Diabetes, 46:2096-2101, 1997.	
	A125	Persson et al., "S-100 protein and neuron-specific enolase in cerebrospinal fluid and serum: markers of cell damage in human central nervous system," Stroke, 18:911-918, 1987.	
LVC	A126	Phanithi et al., "Mild hypothermia mitigates post-ischemic neuronal death following focal cerebral ischemia in rat brain: Immunohistochemical study of Fas, caspase-3 and TUNEL," Neuropathol., 20:273-282, 2000.	

Examiner Signature	<i>Lisa J. Cook</i>	Date Considered	12/29/06
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		Application Number	10/225,882 10/24/03
		Filing Date	08/20/2002 11/14/03
		First Named Inventor	Gunars E. Valkirs eh ah
		Group Art Unit	1632 1641
		Examiner Name	L. Cook
Sheet	15	of	21
		Attorney Docket Number	071949-5408

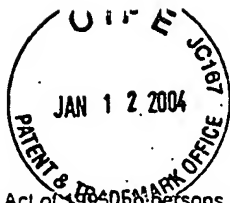
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L/C	A127	Polin et al., "Detection of soluble E-selectin, ICAM-1, VCAM-1, and L-selectin in the cerebrospinal fluid of patients after subarachnoid hemorrhage," J. Neurosurg., 89:559-567, 1998.	
	A128	Prickett et al., "Identification of amino-terminal pro-C-type natriuretic peptide in human plasma," Biochem. Biophys. Res. Commun., 286:513-517, 2001.	
	A129	Quinn et al., "Mapping of antigenic sites in human neuron-specific enolase by expression subcloning," Clin. Chem., 40: 790-795, 1994.	
	A130	Ray et al., "Predictive factors of tumor response and prognostic factors of survival during lung cancer chemotherapy," Cancer Detect. Prev., 22: 293-304, 1998.	
	A131	Rebuzzi et al., "Incremental prognostic value of serum levels of troponin T and C-reactive protein on admission in patients with unstable angina pectoris," Am. J. Cardiol., 82:715-719, 1998.	
	A132	Robey et al., "Binding of C-reactive protein to chromatin and nucleosome core particles," J. Biol. Chem., 259:7311-7316, 1984.	
	A133	Romanic et al., "Matrix metalloproteinase expression increases after cerebral focal ischemia in rats," Stroke, 29:1020-1030, 1998.	
L/C	A134	Rosenberg, "Matrix metalloproteinases in brain injury," J. Neurotrauma, 12:833-842, 1995.	

Examiner Signature	<i>Quisa. X Cook</i>	Date Considered	12/29/06
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		Application Number	10/226-082 10/214,078
		Filing Date	08/20/2002 11/14/03
		First Named Inventor	Gunars E. Valkirs et al.
		Group Art Unit	1632 1641
		Examiner Name	L. Cook
Sheet	16	of	21
		Attorney Docket Number	071949-5408

OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>2</sup>
L/C	A135	Rubattu et al., "The gene encoding atrial natriuretic peptide and the risk of human stroke," Circulation, 100:1722-1726, 1999.	
	A136	Rucinski et al., "Clearance of human platelet factor 4 by liver and kidney: its alteration by heparin," Am. J. Physiol., 251: H800-H807, 1986.	
	A137	Saraste A., "Morphologic criteria and detection of apoptosis," Herz., 24:189-195, 1999.	
	A138	Schabitz et al., "Intraventricular brain-derived neurotropic factor reduces infarct size after focal cerebral ischemia in rats," J.Cereb. Blood Flow Metab., 14: 500-506, 1997.	
	A139	Schaller et al., "Elevated levels of head activator in human brain tumors and in serum of patients with brain and other neurally derived tumors," J.Neuro-Oncol., 6:251-258, 1988.	
	A140	Schwab et al., "Plasma insulin-like growth factor I and IGF binding protein 3 levels in patients with acute cerebral ischemic injury," Stroke, 28:1744-1748, 1997.	
	A141	Seki et al., "Sustained activation of blood coagulation in patients with cerebral thrombosis," A. J. Hematol., 50: 155-160, 1995.	
L/C	A142	Seki et al., "Plasma levels of thrombomodulin and lipoprotein (a) in patients with cerebral thrombosis," Blood Coagul. Fibrinolysis, 8:391-396, 1997.	

Examiner Signature	<i>Olivia X Cook</i>	Date Considered	12/29/06
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		Application Number	10/225,082 10/214,078		
(use as many sheets as necessary)		Filing Date	08/20/2002 11/14/03		
		First Named Inventor	Gunars E. Valkirs et. al.		
		Group Art Unit	1632 1641		
		Examiner Name	L. Cook		
Sheet	17	of	21	Attorney Docket Number	071949-5408

OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>6</sup>
L/C	A143	Shyu et al., "Serum levels of intercellular adhesion molecule-1 and E-selectin in patients with acute ischaemic stroke," J. Neurol., 244:90-93, 1997.	
	A144	Sixma et al., "Von Willebrand factor and the blood vessel wall," Mayo Clin. Proc., 66:628-633, 1991.	
	A145	Skogseid et al., "Increased serum creatine kinase BB and neuron specific enolase following head injury indicates brain damage," Acta Neurochir (Wein), 115: 106-111, 1992.	
	A146	Sorbi et al., "Elevated levels of 92-kd type IV collagenase (Matrix metalloproteinase 9) in giant cell arteritis," Arthritis Rheum., 39:1747-1753, 1996	
	A147	Steiner et al., "Increased levels of soluble adhesion molecules in Type 2 (Non-insulin dependent) diabetes mellitus are independent of glycaemic control," Thromb. Haemost., 72:979-984, 1994.	
	A148	Stockman et al., "Secondary structure and topology of interleukin-1 receptor antagonist protein determined by heteronuclear three-dimensional NMR spectroscopy," Biochemistry, 31:5237-5245, 1992.	
	A149	Stroemer et al., "Cortical protection by localized striatal injection of IL-1ra following cerebral ischemia in the rat," J.Cereb. Blood Flow Metab., 17:597-604, 1997.	
L/C	A150	Suga et al., "Clinical significance of MCP-1 levels in BALF and serum in patients with interstitial lung diseases," Eur. Respir. J., 14:376-382, 1999.	

Examiner Signature	<i>Oliver X Cook</i>	Date Considered	12/29/06
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		Filing Date	08/20/2002 11/14/03
		First Named Inventor	Gunars E. Valkirs et. al.
		Group Art Unit	1632 1641
		Examiner Name	L. Cook
Sheet	18	of	21
		Attorney Docket Number	071949-5408

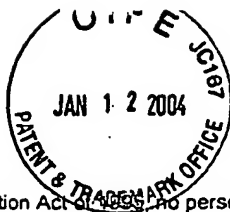
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LVC	A151	Sviri et al., "Brain natriuretic peptide and cerebral vasospasm in subarachnoid hemorrhage: Clinical and TCD correlations," Stroke, 31:118-122, 2000.	
	A152	Switalska et al., "Radioimmunoassay of human platelet thrombospondin: different patterns of thrombospondin and $\beta$ -thromboglobulin antigen secretion and clearance from the circulation," J. Lab. Clin. Med., 106: 690-700, 1985.	
	A153	Takahashi et al., "Tissue factor in plasma of patients with disseminated intravascular coagulation," Am. J. Hematol., 46:333-337, 1994.	
	A154	Takano et al., "Markers of a hypercoagulable state following acute ischemic stroke," Stroke, 23:194-198, 1992.	
	A155	Tateyama et al., "Concentrations and molecular forms of human brain natriuretic peptide in plasma," Biochem. Biophys. Res. Commun., 185:760-7, 1992.	
	A156	Teitz Textbook of Clinical Chemistry, 2 <sup>nd</sup> edition, Carl Burtis and Edward Ashwood eds. Philadelphia: W.B. Saunders and Company, p. 496.	
	A157	Thomas et al., "Serum myelin basic protein, clinical responsiveness, and outcome of severe head injury," Acta Neurochir. Suppl., 28: 93-95, 1979.	
LVC	A158	Tohgi et al., "Coagulation-fibrinolysis abnormalities in acute and chronic phases of cerebral thrombosis and embolism," Stroke, 21: 1663-1667, 1990.	

Examiner Signature	<i>Queen L Cook</i>	Date Considered	12/29/06
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		Application Number	10/225,982 10/214,078
		Filing Date	08/20/2002 11/14/03
		First Named Inventor	Gunars E. Valkirs et al.
		Group Art Unit	1632 1641
		Examiner Name	L. Cook
Sheet 19 of 21		Attorney Docket Number	071949-5408

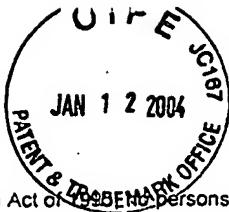
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WC	A159	Tomida et al., "Plasma concentrations of brain natriuretic peptide in patients with subarachnoid hemorrhage," Stroke, 29:1584-1587, 1998.	
	A160	Tousoulis et al., "Von Willebrand factor in patients evolving Q-wave versus non-Q-wave acute myocardial infarction," Int. J. Cardiol., 56:259-262, 1996.	
	A161	Trotter et al., "Immunoreactive myelin proteolipid protein-like activity in cerebrospinal fluid and serum of neurologically impaired patients," Ann. Neurol., 14: 554-558, 1983.	
	A162	Uchiyama et al., "Alterations of platelet, coagulation, and fibrinolysis markers in patients with acute ischemic stroke," Semin. Thromb. Hemost., 23: 535-541, 1997.	
	A163	Usui et al., "β-enolase in blood plasma during open heart surgery," J.Neurol., 123:134-139, 1994.	
	A164	Wada et al., "Poor outcome in disseminated intravascular coagulation or thrombotic thrombocytopenic purpura patients with severe vascular endothelial cell injuries," Am. J. Hematol., 58:189-194, 1998.	
	A165	Wang et al., "Monocyte chemoattractant protein-1 messenger RNA expression in rat ischemic cortex," Stroke, 26:661-665, 1995.	
WC	A166	Wijdicks et al., "Natriuretic peptide system and endothelin in aneurysmal subarachnoid hemorrhage," J. Neurosurg., 87:275-280, 1997.	

Examiner Signature	Olisa. L Cook	Date Considered	12/29/06
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Substitute for form 1449B/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT  (use as many sheets as necessary)		Complete if Known	
		Application Number	10/225,082 10/214,078
		Filing Date	08/20/2002 11/14/03
		First Named Inventor	Gunars E. Valkirs et. al.
		Group Art Unit	1632 1691
		Examiner Name	L. Cook
Sheet	20	of	21
		Attorney Docket Number	071949-5408

OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>2</sup>
LVC	A167	Wilkins et al., "The natriuretic-peptide family," Lancet, 349:1307-1310, 1997.	
	A168	Winnikes et al., "Head activator as a potential serum marker for brain tumor analysis," Eur. J. Cancer, 28:421-424, 1992.	
	A169	Woertgen et al., "Comparison of serial S-100 and NSE serum measurements after severe head injury," Acta Neurochir (Wien), 139: 1161-1165, 1997.	
	A170	Yamagami et al., "Differential production of MCP-1 and cytokine-induced neutrophil chemoattractant in the ischemic brain after transient focal ischemia in rats," J. Leukoc. Biol., 65:744-749, 1999.	
	A171	Yamazaki et al., "Alterations of haemostatic markers in various subtypes and phases of stroke," Blood Coagul., Fibrinolysis, 4:707-712, 1993.	
	A172	Yang et al., "Overexpression of interleukin-1 receptor antagonist in the mouse brain reduces ischemic brain injury," Brain Res. 751: 181-188, 1997.	
	A173	Yap et al., "Contraction to big endothelin-1, big endothelin-2 and big endothelin-3, and endothelin-converting enzyme inhibition in human isolated bronchi," Br. J. Pharmacol., 129:170-7, 2000.	
LVC	A174	Yazdani et al., "Percutaneous interventions after the hemostatic profile of patients with unstable versus stable angina," J. Am. Coll. Cardiol., 30:1284-1287, 1997.	

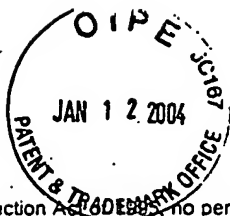
Examiner Signature	<i>Lisa L. Cook</i>	Date Considered	12/29/06
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		Application Number	10/225,982 10/24/03
		Filing Date	08/20/2002 11/14/03
		First Named Inventor	Gunars E. Valkirs et al.
		Group Art Unit	1632 1641
		Examiner Name	L. Coolidge
Sheet	21 of 21	Attorney Docket Number	071949-5408

OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>6</sup>
L/C	A175	Yoneda et al., "Identification of a novel adenylate kinase system in the brain: Cloning of the fourth adenylate kinase," Mol. Brain Res., 62: 187-195, 1998.	
	A176	Yoshimura et al., "Human monocyte chemoattractant protein-1 (MCP-1)," FEBS Lett., 244:487-493, 1989.	
	A177	Yoshitomi et al., "Plasma levels of adrenomedullin in patients with acute myocardial infarction," Clin. Sci. 94:135-9, 1998	
L/C	A178	Zucker et al., "Increased serum stromelysin-1 levels in systemic lupus erythematosus: lack of correlation with disease activity," J.Rheumatol., 26:78-80, 1999.	

Examiner Signature	<i>Oliver Klock</i>	Date Considered	12/29/06
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<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b> (use as many sheets as necessary)		Application Number	10/714,078
		Filing Date	11/14/2003
		First Named Inventor	Valkirs et al.
		Group Art Unit	4651 1641
		Examiner Name	L. Cook
Sheet 1 of 1	Attorney Docket Number	071949-5408	

U.S. PATENT DOCUMENTS						
Examiner Initials*	Cite No. <sup>1</sup>	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number	Kind Code <sup>2</sup> (if known)			
L/C	A1	5352587		Chang et al.	10-04-1994	
L/C	A2	5422393		Bricker et al.	06-06-1995	

FOREIGN PATENT DOCUMENTS							
Examiner Initials*	Cite No. <sup>1</sup>	Foreign Patent Document			Name of Patentee or Applicant of Cited Documents	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Office <sup>3</sup>	Number <sup>4</sup>	Kind Code <sup>5</sup> (if known)			

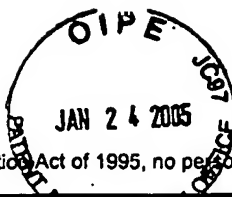
NON PATENT LITERATURE DOCUMENTS				
Examiner Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.		
L/C	A3	International Search Report and the Written Opinion of the International Searching Authority from PCT Application No. PCT/US04/12024.		

Examiner Signature	<i>Lisa. X Cook</i>	Date Considered	12/29/06
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Substitute for form PTO/SB/08 <b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b> Date Submitted: January 20, 2005 (Use as many sheets as necessary)		<b>Complete if Known</b>	
		Application Number	10/672,977 10/21/03
Sheet 1 of 1		Filing Date	09/26/2003 11/14/03
		First Named Inventor	Gunars Valkirs
		Group Art Unit	3670-1641
		Examiner Name	Unknown L. Cook
		Attorney Docket Number	071949-5408

U.S. PATENT DOCUMENTS						
Examiner Initials*	Cite No. <sup>1</sup>	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number	Kind Code <sup>2</sup> (if known)			
L/C	A1	5786163		Hall	07-28-1998	
	A2	6627457		Pandian et al.	09-30-2003	
L/C	A3	6670138		Gonzalez-Zulueta et al.	12-30-2003	

FOREIGN PATENT DOCUMENTS								
Examiner Initials*	Cite No. <sup>1</sup>	Foreign Patent Document			Name of Patentee or Applicant of Cited Documents	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T <sup>6</sup>
		Office <sup>3</sup>	Number <sup>4</sup>	Kind Code <sup>5</sup> (if known)				

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L/C	A4	Huttunen et al., "Coregulation of neurite outgrowth and cell survival by amphotericin and S100 proteins through receptor for advanced glycation end products (RAGE) activation. The Journal of Biological Chemistry, 275:40096-40105, 2000.	
	A5	Mussack et al., Early cellular brain damage and systemic inflammatory response after cardiopulmonary resuscitation or isolated severe head trauma: a comparative pilot study on common pathomechanisms. Resuscitation, 49:193-199, 2001.	
	A6	Yakovlev et al., Activation of CPP32-Like caspases contributes to neuronal apoptosis and neurological dysfunction after traumatic brain injury. The Journal of Neuroscience, 17(19): 7415-7424, 1997.	
	A7	International Search Report for international application No. PCT/US04/26984	
L/C	A8	Notice of References Cited, PTO-892, Part of Paper No. 20041202 from U.S. Application No. 10/225,082 filed August 20, 2002.	


Examiner Signature	<i>Lisa L. Cook</i>	Date Considered	12/29/06
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Application Number				10/714,078	
Filing Date				11/14/2003	
First Named Inventor				Gunars E. Valkirs	
Group Art Unit				<del>1651</del> 1641	
Examiner Name				Unknown L. Cook	
Attorney Docket Number				071949-5408	
Sheet	1	of	1		

## U.S. PATENT DOCUMENTS

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## FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No. <sup>1</sup>	Foreign Patent Document		Name of Patente or Applicant of Cited Documents	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T <sup>6</sup>
		Office <sup>3</sup>	Number <sup>4</sup> <i>(if known)</i>				

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INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT

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1

of

1

## Complete if Known

Application Number	10/714,078
Filing Date	11/14/2003
First Named Inventor	VALKIRS
Group Art Unit	1651 1641
Examiner Name	L. Cook
Attorney Docket Number	071949-5408

## U.S. PATENT DOCUMENTS

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		Office <sup>3</sup>	Number <sup>4</sup>	Kind Code <sup>5</sup> (if known)				

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L/C	A1	Harter et al., Caspase-3 activity is present in cerebrospinal fluid from patients with traumatic brain injury. Journal of Neuroimmunology, 121:76-78, 2001.	

Examiner  
Signature

L. Cook

Date  
Considered

12/29/06

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**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**

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Sheet

1

of

1

Application Number

10/714,078

Filing Date

11/14/2003

First Named Inventor

Gunars E. Valkirs

Group Art Unit

1651 1641

Examiner Name

Unassigned L. Cook

Attorney Docket Number

071949-5408

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		Number	Kind Code <sup>2</sup> (if known)			
L/C	A1	5,206,140		Marder et al.	04-27-1993	
L/C	A2	6,309,888		Holvoet et al.	10-30-2001	
L/C	A3	6,461,828		Stanton et al.	10-08-2002	

## U.S. PATENT APPLICATION DOCUMENTS

Examiner Initials*	Cite No. <sup>1</sup>	U.S. Patent Application Document		Name of Patentee or Applicant of Cited Document	Filing Date of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
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		Office <sup>3</sup>	Number <sup>4</sup>	Kind Code <sup>5</sup> (if known)				

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L/C	A4	FONAROW et al., "Combining Natriuretic Peptides and Necrosis Markers in Determining Prognosis in Heart Failure," Reviews in Cardiovascular Medicine, 2003, Suppl. 4, Vol. 4	
L/C	A5	RICHARDS et al., "Neuroendocrine prediction of left ventricular function and heart failure after acute myocardial infarction," Heart, 1999, pp. 114-120, Vol. 81	
L/C	A6	SAADY et al., "Left appendage: structure function, and role in thromboembolism," Heart, 1999, pp. 547-555, Vol. 82	

Examiner Signature

Lisa L. Cook

Date Considered

12/29/06

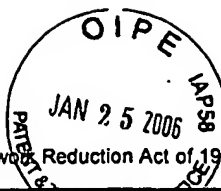
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		Application Number	10/714,078
		Filing Date	11/14/2003
		First Named Inventor	Gunars E. Valkirs
		Group Art Unit	1651 1641
Examiner Name	Unassigned	L Cook	
Attorney Docket Number	071949-5408		

Sheet 1 of 2

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Examiner Initials*	Cite No. <sup>1</sup>	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
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		Office <sup>3</sup>	Number <sup>4</sup>	Kind Code <sup>5</sup> (if known)				
L/C	A1	WO	02/083913		Biosite Diagnostics, Inc.	10-24-2002		

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L/C ①	A2	CASSIN et al., <i>E' realizzabile una strategia operative piu efficace per la gestione in urgenza del paziente con dolore toracico acuto?</i> , Ital Heart J Suppl, Feb. 2000, pp. 186-201, Vol. 1			
L/C	A3	FUTTERMAN et al., <i>Novel Markers in the Acute Coronary Syndrome: BNP, IL-6, PAPP-A</i> , American Journal of Critical Care, March 2002, pp. 168-172, Vol. 11, No. 2			
L/C	A4	HUNT et al., <i>Immunoreactive amino-terminal pro-brain natriuretic peptide (NT-PROBNP): a new marker of cardiac impairment</i> , Clinical Endocrinology, 1997, pp. 287-296, Vol. 47			

① only English abstract considered.

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<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  (use as many sheets as necessary)				Application Number	10/714,078
				Filing Date	11/14/2003
				First Named Inventor	Gunars E. Valkirs
				Group Art Unit	1651-1641
				Examiner Name	Unassigned L. Cool
Sheet	2	of	2	Attorney Docket Number	071949-5408

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L/C	A5	SAGNELLA et al., Measurement and significance of circulating natriuretic peptides in cardiovascular disease, Clinical Science, Nov. 1998, pp. 519-529, Vol. 95, No. 5			
L/C	A6	SONEL et al., Prospective Study Correlating Fibrinopeptide A, Troponin I, Myoglobin, and Myosin Light Chain Levels with Early and Late Ischemic Events in Consecutive Patients Presenting to the Emergency Department with Chest Pain, Circulation, Sep. 5, 2000, pp. 1107-1113, Vol. 102, No. 10			
X					

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1		of		1	
Application Number		10/714,078			
Filing Date		11/14/2003			
First Named Inventor		Gunars E. Valkirs			
Group Art Unit		1651 1641			
Examiner Name		Unknown LCOOK			
Attorney Docket Number		071949-5408			

U.S. PATENT DOCUMENTS						
Examiner Initials*	Cite No. <sup>1</sup>	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number	Kind Code <sup>2</sup> (if known)			
LYC	A1	2003/0022235		Dahlen et al.	01-30-2003	
LYC	A2	5,290,678		Jackowski	03-01-1994	

U.S. PATENT APPLICATION DOCUMENTS						
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